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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MACAULEY, SHERIDAN R	
ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,480	FREEZE ET AL.	
	Examiner	Art Unit	
	Sheridan R. MacAuley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *123-150* is/are pending in the application.

4a) Of the above claim(s) *144-150* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *123-143* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 123-150 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 123-143, in the reply filed on June 15, 2007 is acknowledged. The restriction requirement is deemed proper and is therefore made FINAL.

2. Claims 144-150 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 123-143 are examined on the merits in this office action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 142 and 143 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

6. It is apparent that the claimed antibodies (mAbEE4.1, mAbGB3.1, mAbB2.6, and mAbEH2.7) are required to practice the claimed invention. As such the biological material must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not obtainable or available, the requirement of 35 USC 112, first paragraph may be satisfied by a deposit of the biological material.

7. The process disclosed in the specification does not appear to be repeatable, it is not clear that the invention will work with commonly available material and it is not apparent if the biological material are both known and readily available to the public.

8. If a deposit has been made under the terms of the Budapest Treaty, then a statement, affidavit or declaration by applicant, or a statement by an attorney of record over his or her signature and registration number, or someone empowered to make such a statement, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

9. If a deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, applicant may provide assurance of compliance by statement, affidavit or declaration, or by someone empowered to make the same, or by a statement by an attorney of record over his or her signature and registration number showing that:

a. during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;
b. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

c. the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last requires or for the enforceable life of the patent, whichever is longer;
d. a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and
e. the deposit will be replaced if it should ever become inviable.

10. Claim 136 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying a test agent which reduces binding to specific carboxylated glycans, does not reasonably provide enablement for identifying the test agent as reducing inflammation or cancer. Claim 136 recites the method of claim 135 (as described below) further comprising (d) identifying said test agent as reducing inflammation or cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the instant case, those factors deemed most relevant are the quantity of

experimentation necessary, the state of the prior art, the predictability or unpredictability of the art and the breadth of the claims.

The disclosure is not enabling for identifying a test agent as reducing inflammation or cancer because it does not present enough direction and guidance for one skilled in the art to use the invention with a reasonable expectation of success without undue experimentation. Although the disclosure provides guidance for the identification of an agent which reduces inflammation or cancer cell growth related to the binding of the proteins annexin I, S100A8/A9 and amphoterin, the disclosure does not provide any guidance or working examples to direct one to the development of a screening method that would identify any test agent that reduces inflammation or cancer. The state of the prior art indicates that the identification of an agent that reduces cancer in vitro does not adequately predict the effect of the drug when used to treat a cancer patient in vivo (see Zips et al., 2005, In vivo, 19:1-8, p. 3, col. 2, par. 3). One would thus be required to screen a test agent in vivo to identify such an agent as reducing cancer, requiring undue experimentation for one of ordinary skill in the art to use the invention as claimed. Further, applicant discloses in the specification that a cascade of molecular events are involved in the production of an inflammatory response, particularly in the recruitment of leukocytes (see specification, pp. 1-3). There is no guidance provided to detect agents that reduce inflammation by pathways other than those disclosed. Due to the complexity of molecular events involved in the production of an inflammatory response, one would be unable to predict whether a test agent would reduce inflammation without undue experimentation. Given these facts,

one skilled in the art would be unable to predict whether the claimed method for the identification of agents that reduce inflammation or cancer could be performed with a reasonable expectation of success.

Therefore, the disclosure of the instant application does not enable one skilled in the art to use the invention as claimed.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 123-128, 130, 131, 133 and 134 are rejected under 35 U.S.C. 102(b) as being anticipated by Varki et al. (US 5,449,781). Claim 123 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing: (i) a molecule comprising a carboxylated glycan; (ii) biotinylated diamino pyridine (BAP); and (iii) an exoglycosidase; (b) conjugating said molecule to said BAP to produce a BAP-glycan conjugate; (c) treating said BAP-glycan conjugate with said exoglycosidase to produce a first treated BAP-glycan conjugate comprising a first anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (d) isolating said first anionic BAP-glycan conjugate, thereby purifying a carboxylated glycan. Claim 124 recites the method of claim 123, further comprising the steps of: (e) treating said first anionic BAP-glycan conjugate produced in step (e) or (d) with an exoglycosidase to produce a

second anionic treated BAP-glycan conjugate comprising a second anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (f) isolating said second anionic BAP-glycan conjugate, thereby purifying a carboxylated glycan. Claim 125 recites the method of 124, further comprising repeating steps (e) and (f) from 1 to 10 times. Claim 126 recites the method of claim 123 wherein said isolating comprises fractionating by ion exchange chromatography. Claim 127 recites a carboxylated glycan purified by the method of claim 123. Claim 128 recites the glycan of claim 127, wherein the molecule is a glycoprotein or polysaccharide, specifically a receptor for advanced glycation end products (RAGE). Claim 130 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing a molecule comprising a carboxylated glycan; (b) isolating from said molecule a first anionic glycan containing from 1 to 4 negative charges; and (c) desialylating said isolated first anionic glycan to produce a desialylated anionic glycan containing from 1 to 4 negative charges, thereby purifying a carboxylated glycan. Claim 131 recites the method of claim 130, further comprising (d) isolating from said first disialylated anionic glycan, thereby purifying a carboxylated glycan. Claims 133 and 134 recite a carboxylated glycan purified by the method of claim 130, specifically wherein the molecule is a glycoprotein or a polysaccharide.

13. Varki teaches a method for purifying a carboxylated glycan (e.g. those containing siacylic acid residues) comprising conjugating a carboxylated glycan with BAP; treating the BAP-glycan conjugate with an exoglycosidase (sialidase); and isolating the BAP-glycan conjugate (by HPLC), thereby purifying the glycan (col. 9, line 51-col. 10, line 8,

col. 10, lines 47-62). Although Varki does not specifically teach that the BAP-glycan conjugate has 1-2 negative charges per molecule, the process may use a number of conjugates that would inherently have the claimed charges. Varki teaches that the BAP-glycan conjugate produced by the claimed process may be further treated with exoglycosidases to produce further BAP-glycan conjugates, which may further be purified, and that this process may be repeated one or more times (col. 11, lines 7-26). Varki teaches that isolating the BAP-glycan conjugate may comprise ion exchange chromatography (col. 11, lines 53-57). The method of Varki comprises the steps of providing a molecule comprising a carboxylated glycan (the BAP-glycan conjugate); isolating form the molecule a first anionic glycan containing from 1-4 charges; desialylating the isolated first anionic glycan to produce a desialylated anionic glycan containing from 1-4 negative charges; and isolating from the first glycan a second anionic glycan containing from 1-4 negative charges (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62; col. 11, lines 53-57). Varki teaches a purified carboxylated glycan, and that the molecule which comprises the glycan can be a polysaccharide (col. 9, line 66-col. 10, line 8).

14. Therefore, Varki anticipates all of the limitations of the cited claims.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 123-128, 130-135, 137, 138, 140 and 141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Varki et al. (US 5,449,781) in view of Schmidt et al. (Biochimica et Biophysica Acta, 2000, 99-111) and Hodges et al. (US 5,738,996). Claim 123 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing: (i) a molecule comprising a carboxylated glycan; (ii) biotinylated diamino pyridine (BAP); and (iii) an exoglycosidase; (b) conjugating said molecule to said BAP to produce a BAP-glycan conjugate; (c) treating said BAP-glycan conjugate with said

exoglycosidase to produce a first treated BAP-glycan conjugate comprising a first anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (d) isolating said first anionic BAP-glycan conjugate, thereby purifying a carboxylated glycan. Claim 124 recites the method of claim 123, further comprising the steps of: (e) treating said first anionic BAP-glycan conjugate produced in step (e) or (d) with an exoglycosidase to produce a second anionic treated BAP-glycan conjugate comprising a second anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (f) isolating said second anionic BAP-glycan conjugate, thereby purifying a carboxylated glycan. Claim 125 recites the method of 124, further comprising repeating steps (e) and (f) from 1 to 10 times. Claim 126 recites the method of claim 123 wherein said isolating comprises fractionating by ion exchange chromatography. Claim 127 recites a carboxylated glycan purified by the method of claim 123. Claim 128 recites the glycan of claim 127, wherein the molecule is a glycoprotein or polysaccharide. Claim 130 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing a molecule comprising a carboxylated glycan; (b) isolating from said molecule a first anionic glycan containing from 1 to 4 negative charges; and (c) desialylating said isolated first anionic glycan to produce a desialylated anionic glycan containing from 1 to 4 negative charges, thereby purifying a carboxylated glycan. Claim 131 recites the method of claim 130, further comprising (d) isolating from said first disialylated anionic glycan, thereby purifying a carboxylated glycan. Claim 132 recites the method of claim 130, further comprising a step of treating the molecule with a proteinase enzyme prior to step (a). Claims 133 and 134 recite a carboxylated glycan

purified by the method of claim 130, specifically wherein the molecule is a glycoprotein or a polysaccharide. Claim 135 recites a method for identifying a test agent as reducing specific binding of a polypeptide to a carboxylated glycan, comprising: (a) providing: (i) a carboxylated glycan purified by the method of claim 1; (ii) an antibody that specifically binds to said carboxylated glycan; and (iii) a test agent; (b) contacting said purified carboxylated glycan, said antibody, and said test agent; and (c) detecting a reduction in the level of binding of said antibody to said carboxylated glycan in the presence of said test agent compared to in the absence of said test agent, thereby identifying said test agent as reducing specific binding of a polypeptide to a carboxylated glycan. Claim 137 recites the method of claim 135, wherein the glycan is attached to a solid surface. Claim 138 recites the method of claim 135 wherein the molecule is a glycoprotein or polysaccharide. Claims 140 and 141 recite the method of claim 135, wherein the antibody is monoclonal, specifically an IgG antibody.

19. Varki teaches a method for purifying a carboxylated glycan (e.g. those containing siacylic acid residues) comprising conjugating a carboxylated glycan with BAP; treating the BAP-glycan conjugate with an exoglycosidase (sialidase); and isolating the BAP-glycan conjugate (by HPLC), thereby purifying the glycan (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62). Although Varki does not specifically teach that the BAP-glycan conjugate has 1-2 negative charges per molecule, the process may use a number of conjugates that would inherently have the claimed charges. Varki teaches that the BAP-glycan conjugate produced by the claimed process may be further treated with exoglycosidases to produce further BAP-glycan conjugates, which may further be

purified, and that this process may be repeated one or more times (col. 11, lines 7-26). Varki teaches that isolating the BAP-glycan conjugate may comprise ion exchange chromatography (col. 11, lines 53-57). The method of Varki comprises the steps of providing a molecule comprising a carboxylated glycan (the BAP-glycan conjugate); isolating form the molecule a first anionic glycan containing from 1-4 charges; desialylating the isolated first anionic glycan to produce a desialylated anionic glycan containing from 1-4 negative charges; and isolating from the first glycan a second anionic glycan containing from 1-4 negative charges (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62; col. 11, lines 53-57). Varki teaches a purified carboxylated glycan, and that the molecule which comprises the glycan can be a polysaccharide (col. 9, line 66-col. 10, line 8). Varki teaches a method for screening recombinant protein libraries using the BAP-conjugated glycans to identify proteins that bind to the saccharides (col. 7, lines 17-25). Varki teaches that IgG antibodies can be produced which specifically bind to the purified glycans (col. 7. lines 8-13).

20. Varki does not teach a step of treating the molecule with a proteinase prior to step (a) of the process recited in claim 130. Varki does not specifically teach a method for identifying a test agent that reduces specific binging of a polypeptide to a carboxylated glycan.

21. Hodges teaches a test method wherein a labeled antigen, which may be immobilized, is bound to an antibody and a test agent, wherein the reduction of the level of binding of the antibody to the antigen is detected and is indicative of specific binding of the test agent to the antigen (col. 13, lines 28-44, col. 14, lines 6-15).

22. At the time of the invention, a method for purifying a carboxylated glycan comprising nearly all of the claimed elements was known, as taught by Varki. It was further known at the time of the invention that tests could be conducted to detect the specific binding of a test agent by measuring the reduction in the specific binding of an antibody, as taught by Hodges. The treatment of a composition comprising an oligosaccharide with a protease prior to purification would have been a matter of routine experimentation for one of ordinary skill in the art in order to remove any proteins that may be bound to the oligosaccharides. One or ordinary skill in the art would have been motivated to combine these teachings because Varki teaches that it would be desirable to use the methods to screen for proteins which bind to the saccharides, and that the methods enable the production of antibodies specific for the saccharides (col. 7, lines 18-21). Hodges teaches a method using antibodies to screen for proteins that bind to an antigen. One would therefore have recognized that it would be desirable to use the methods of Hodges in combination with the method taught by Varki. One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings because Varki teaches all of the required elements, and Hodges teaches simplified screening methods. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

23. Claims 123-135 and 137-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Varki et al. (US 5,449,781) in view of Hodges et al. (US 5,738,996),

as applied to claims 123-128, 130-135, 137, 138, 140 and 141 above, and further in view of Schmidt et al. (Biochimica et Biophysica Acta, 2000, 99-111). Claim 123 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing: (i) a molecule comprising a carboxylated glycan; (ii) biotinylated diamino pyridine (BAP); and (iii) an exoglycosidase; (b) conjugating said molecule to said BAP to produce a BAP-glycan conjugate; (c) treating said BAP-glycan conjugate with said exoglycosidase to produce a first treated BAP-glycan conjugate comprising a first anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (d) isolating said first anionic BAP-glycan conjugate, thereby purifying a carboxylated glycan. Claim 124 recites the method of claim 123, further comprising the steps of: (e) treating said first anionic BAP-glycan conjugate produced in step (e) or (d) with an exoglycosidase to produce a second anionic treated BAP-glycan conjugate comprising a second anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (f) isolating said second anionic BAP-glycan conjugate, thereby purifying a carboxylated glycan. Claim 125 recites the method of 124, further comprising repeating steps (e) and (f) from 1 to 10 times. Claim 126 recites the method of claim 123 wherein said isolating comprises fractionating by ion exchange chromatography. Claim 127 recites a carboxylated glycan purified by the method of claim 123. Claims 128 and 129 recite the glycan of claim 127, wherein the molecule is a glycoprotein or polysaccharide, specifically a receptor for advanced glycation end products (RAGE). Claim 130 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing a molecule comprising a carboxylated glycan; (b) isolating from said molecule a first

anionic glycan containing from 1 to 4 negative charges; and (c) desialylating said isolated first anionic glycan to produce a desialylated anionic glycan containing from 1 to 4 negative charges, thereby purifying a carboxylated glycan. Claim 131 recites the method of claim 130, further comprising (d) isolating from said first disialylated anionic glycan, thereby purifying a carboxylated glycan. Claim 132 recites the method of claim 130, further comprising a step of treating the molecule with a proteinase enzyme prior to step (a). Claims 133 and 134 recite a carboxylated glycan purified by the method of claim 130, specifically wherein the molecule is a glycoprotein or a polysaccharide. Claim 135 recites a method for identifying a test agent as reducing specific binding of a polypeptide to a carboxylated glycan, comprising: (a) providing: (i) a carboxylated glycan purified by the method of claim 1; (ii) an antibody that specifically binds to said carboxylated glycan; and (iii) a test agent; (b) contacting said purified carboxylated glycan, said antibody, and said test agent; and (c) detecting a reduction in the level of binding of said antibody to said carboxylated glycan in the presence of said test agent compared to in the absence of said test agent, thereby identifying said test agent as reducing specific binding of a polypeptide to a carboxylated glycan. Claim 137 recites the method of claim 135, wherein the glycan is attached to a solid surface. Claims 138 and 139 recite the method of claim 135 wherein the molecule is a glycoprotein or polysaccharide, specifically RAGE. Claims 140-141 recite the method of claim 135, wherein the antibody is monoclonal, specifically an IgG antibody.

24. Varki teaches a method for purifying a carboxylated glycan (e.g. those containing siacylic acid residues) comprising conjugating a carboxylated glycan with BAP; treating

the BAP-glycan conjugate with an exoglycosidase (sialidase); and isolating the BAP-glycan conjugate (by HPLC), thereby purifying the glycan (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62). Although Varki does not specifically teach that the BAP-glycan conjugate has 1-2 negative charges per molecule, the process may use a number of conjugates that would inherently have the claimed charges. Varki teaches that the BAP-glycan conjugate produced by the claimed process may be further treated with exoglycosidases to produce further BAP-glycan conjugates, which may further be purified, and that this process may be repeated one or more times (col. 11, lines 7-26). Varki teaches that isolating the BAP-glycan conjugate may comprise ion exchange chromatography (col. 11, lines 53-57). The method of Varki comprises the steps of providing a molecule comprising a carboxylated glycan (the BAP-glycan conjugate); isolating form the molecule a first anionic glycan containing from 1-4 charges; desialylating the isolated first anionic glycan to produce a desialylated anionic glycan containing from 1-4 negative charges; and isolating from the first glycan a second anionic glycan containing from 1-4 negative charges (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62; col. 11, lines 53-57). Varki teaches a purified carboxylated glycan, and that the molecule which comprises the glycan can be a polysaccharide (col. 9, line 66-col. 10, line 8). Varki teaches a method for screening recombinant protein libraries using the BAP-conjugated glycans to identify proteins that bind to the saccharides (col. 7, lines 17-25). Varki teaches that IgG antibodies can be produced which specifically bind to the purified glycans (col. 7. lines 8-13).

25. Hodges teaches a test method wherein a labeled antigen, which may be immobilized, is bound to an antibody and a test agent, wherein the reduction of the level of binding of the antibody to the antigen is detected and is indicative of specific binding of the test agent to the antigen (col. 13, lines 28-44, col. 14, lines 6-15).

26. It would have been obvious at the time of the invention to combine the teachings of Varki and Hodges to develop the claimed methods, as discussed above. However, neither Varki nor Hodges teaches that the molecule comprising the glycan is a glycoprotein such as RAGE.

27. Schmidt teaches that RAGE is receptor protein for advanced glycation end products (AGEs; abstract, p. 100, col. 2, par. 2).

28. At the time of the invention, methods for purifying a carboxylated glycan and identifying a test agent comprising nearly all of the claimed elements were known, as taught by Varki and Hodges. The RAGE protein was also known at the time of the invention, as taught by Schmidt. One of ordinary skill in the art would have been motivated to combine these teachings because Varki teaches that it would be desirable to produce BAP conjugates with glycoproteins as well as oligosaccharides (col. 1, lines 48-59). One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings because Varki teaches that the process may be used to purify any molecule with a bound glycan, such as RAGE. Moreover, RAGE was a known protein at the time of the invention. The discovery that a previously protein has previously unknown elements (e.g. bound glycans) does not render the use of that protein with a known method novel. It would therefore have been obvious to one of

ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

29. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan R. MacAuley whose telephone number is (571) 270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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